AD_____

Award Number: W81XWH-12-1-0170

TITLE: Prospective Evaluation of Intraprostatic Inflammation and Focal Atrophy as a Predictor of Risk of High-Grade Prostate Cancer and Recurrence after Prostatectomy

PRINCIPAL INVESTIGATOR: Elizabeth A. Platz

CONTRACTING ORGANIZATION: Johns Hopkins Bloomberg School of Public Health
Baltimore, MD 21205

REPORT DATE: July 2013

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 0704-0188*



| 1. REPORT DATE | 2. REPORT TYPE | 3. DATES COVERED |
|---|---|---|
| July 2013 | Annual | 1 July 2012 - 30 June 2013 |

**4. TITLE AND SUBTITLE**

Prospective Evaluation of Intraprostatic Inflammation and Focal Atrophy as a Predictor of Risk of High-Grade Prostate Cancer and Recurrence after Prostatectomy

**5a. CONTRACT NUMBER**

**5b. GRANT NUMBER**
W81XWH-12-1-0170

**5c. PROGRAM ELEMENT NUMBER**

**6. AUTHOR(S)**
Elizabeth A. Platz

E-Mail: eplatz@jhsph.edu

**5d. PROJECT NUMBER**

**5e. TASK NUMBER**

**5f. WORK UNIT NUMBER**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

Johns Hopkins Bloomberg School of Public Health
Baltimore, MD 21205

**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

**10. SPONSOR/MONITOR'S ACRONYM(S)**

**11. SPONSOR/MONITOR'S REPORT NUMBER(S)**

**12. DISTRIBUTION / AVAILABILITY STATEMENT**
Approved for Public Release; Distribution Unlimited

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
We are evaluating, in two nested case-control studies, intraprostatic inflammation and focal atrophy, a prostate lesion that is often inflamed, as tissue markers for risk of future diagnosis of high-grade prostate cancer, and for prognosis at the time of surgery for clinically localized prostate cancer. For prostate cancer incidence, in Year 1, we developed the source population, prostate cancer case, and control definitions for this work, selected all prostate cancer cases and 2 controls per case who were frequency matched on age, race, and treatment arms for the two trials. We pulled prostate biopsy tissue samples from the PCPT biorepository and cut and mounted sections from paraffin-embedded prostate tissue biopsy core per man onto slides. We imaged H&E stained section of prostate tissue biopsy cores and uploaded the images for remote review. For prostate cancer recurrence, in Year 1, we pulled the recurrence TMAs, cut and mounted TMA sections, and H&E stained them. We have optimized the IHC staining for the immune markers for the prostate tissue biopsies and are doing the same for the recurrence TMAs. Our work is progressing per the Statement of Work.

**15. SUBJECT TERMS**

None provided.

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | USAMRMC |
| U | U | U | UU | 5 | 19b. TELEPHONE NUMBER *(include area code)* |

## Table of Contents

**Page**

**INTRODUCTION:** With respect to healthy men, at this time, we do not know how to prevent the development of prostate cancer that has the potential to be aggressive, nor do we have a tool to identify men who would most benefit from preventive interventions for aggressive disease. With respect to men with early prostate cancer, at this point, we still cannot predict with certainty which men are more likely to suffer and die of their prostate cancer after prostatectomy. In this population-based research project, we are directly addressing these major problems. We are evaluating, in two nested case-control studies, intraprostatic inflammation and focal atrophy, a prostate lesion that is often inflamed, as tissue markers for risk of future diagnosis of high-grade prostate cancer, and for prognosis at the time of surgery for clinically localized prostate cancer. Our overall hypotheses are: 1) Chronic intraprostatic inflammation is a cause of prostate cancer that is more likely to be aggressive and recur. 2) Focal atrophy, a prostate lesion that is often inflamed, is a risk and prognostic indicator.

**BODY:** This work is being performed collaboratively by three institutions: Johns Hopkins Bloomberg School of Public Health, Fred Hutchinson Cancer Research Center, and the University of Colorado, Denver School of Medicine. We obtained all required IRB approvals for both the PCPT-SELECT linked study on prostate cancer incidence and the Brady prostate cancer recurrence study, including from the DOD IRB **(Task 1 completed)**. A Materials Use Agreement and Data Use Agreement were executed between SWOG and Johns Hopkins University for the PCPT-SELECT linked study. Drs. Platz and De Marzo previously created the prostate cancer recurrence case-control study (in part with prior DOD funding) and associated TMAs. This TMA set is now part of the Prostate Cancer Biorepository Network. For equitable use and tracking purposes, we applied for access to these TMAs and received approval from the PCBN.

*Prostate cancer incidence:* We developed the source population, prostate cancer case, and control definitions for this work. Based on those definitions, we identified eligible men who participated in both the PCPT and SELECT. From the source population, we identified all prostate cancer cases and selected two controls per case who were frequency matched on age, race, and treatment arms for the two trials. The expected sample size for this work was 100 cases and 200 controls. Tissue was sufficient for 291 of the men **(Task 2 completed)**. We pulled prostate biopsy tissue samples from the PCPT biorepository for the 291 men. We cut and mounted 5 sections from one paraffin-embedded prostate tissue biopsy core per man onto slides. These slides were shipped in batches to Johns Hopkins (total of 31 boxes). We received and accessioned the slides. We imaged the 6th H&E stained section of the paraffin-embedded prostate tissue biopsy core per man and uploaded it into a program for remote review **(Task 3, items a-d completed)**. *Prostate cancer recurrence:* The Brady recurrence nested case-control study already exists; no additional work was needed to define the study population, cases, or controls. We pulled the recurrence TMAs (N=16 TMAs, which includes 524 cases and 524 controls) and cut and mounted 6 TMA sections. H&E stained one TMA section **(Task 5, a-c completed)**.

We have not encountered major barriers. We have optimized the IHC staining for the immune markers for the prostate tissue biopsies and are in the process of doing the same for the recurrence TMAs. Our immediate next steps are: 1) IHC staining of the slides for the immune markers and imaging of those slides for the 291 men in PCPT-SELECT (a total of 1,455 slides) and the 16 TMAs in the Brady recurrence set (a total of 80 slides) (Task 3 e-f, Task 5 d-e). 2) Training the pathology fellow (Dr. Ibrahim Kulac) who during August and September 2013 will review and score the stained and imaged slides for inflammation, focal atrophy, and the immune markers.

**KEY RESEARCH ACCOMPLISHMENTS:** None to date, as consistent with the Statement of Work.

**REPORTABLE OUTCOMES:** Through this work, we developed a resource for prostate cancer researchers: a new cohort derived from the linkage of the PCPT and SELECT trials. This cohort consists of men who were negative for prostate cancer on PCPT end-of-study biopsy and who then enrolled in SELECT. Linking these 2 cohorts is the ONLY epidemiologically sound approach for prospectively testing the association of tissue markers in men without an indication for biopsy or surgery with prostate cancer incidence – at this time and in the foreseeable future. Access to this linked resource is via SWOG (http://swog.org/Visitors/Biorepository/).

**CONCLUSION:** None to date, as consistent with the Statement of Work.

**REFERENCES:** None

**APPENDICES:** None

**SUPPORTING DATA:** None